The Applicant has included this language to further exemplify the features of the Applicant's invention which distinguish the pending claims from Hoffman et al. However, the inclusion of a "sufficient number of oligo [meth-]acrylamide derivative side chains" to form a gel is an inherent result of following the method described in the specification, and therefore of the reversible gels formed thereby, and is therefore cannot be considered new matter. The specification has further been amended to remove the statement that the reaction solvent is non-aqueous, preferably a hydrocarbon, for example chloroform, dichloromethane, N,N-dimethylformamide or combinations thereof, as the placement of this statement was a typographical error, as it actually applies to the first step of the procedure described above it.

Claim 31 has been amended to recite the limitation of this inherent property. No new matter is added thereby. Pursuant to rule 121(c)(3), the version of the amended claims to show changes made is submitted in a separate paper enclosed herein.

REMARKS

The Examiner has asserted that the Applicant has still not distinguished the pending claims from Sassi and Hoffman. With regard to Sassi, the Examiner asserts that Sassi et al. disclose "more than one example in which the amount of acrylamide, embraced by the applicant's hydrophilic comonomer is less than about 10 mole percent as required by the claims." This assertion is simply false. In fact, since both acrylamide and all hydrogen bonding N-substituted acrylamide derivatives taught by Sassi are hydrophilic, all of Sassi's systems are 100% hydrophilic. As the Applicant previously pointed out, with respect to hydrogen bonding, Sassi is operating with the exact opposite mechanism of the Applicant's method, and therefore needs a lot of acrylamide to form sufficient hydrogen bonds to form a gel. Since Sassi has defined "acrylamide" to include acrylamide and all its N-substituted derivatives (see the definition at column 3, lines 3-6), the relevant inquiry with respect to which of Sassi's "acrylamides" are analogous to

the Applicant's hydrophilic comonomer is whether or not any particular acrylamide disclosed by Sassi is hydrophilic. In each of the examples provided by Sassi, the amount of hydrophilic acrylamide is well in excess of the Applicant's claimed range of between 1 and 10 percent. For example, in example 1, Sassi uses a 50:50 blend of AA and AG. Both of these components are hydrophilic. So in this example, as in all of the remaining examples, Sassi teaches a system that is 100% hydrophilic, well outside the Applicant's claimed range. The Applicant hereby requests that, if the Examiner believes one of the examples does teach a range outside of these parameters, the Examiner specifically point out which example.

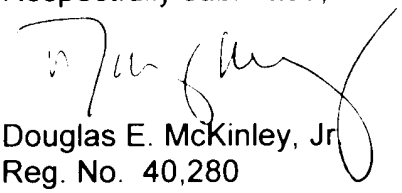
With regard to Hoffman, the Examiner asserts that "it is immaterial whether or not the specific conditions of Hoffman resulted in a gel formation under the conditions of Hoffman." Since the Applicant specifically requires gel formation in all pending claims, the Applicant can only wonder how the fact that Hoffman does NOT form a gel can possibly be considered "immaterial." Nevertheless, the Applicant has amended the specification to make clear that in order to form a gel, a sufficient number of oligo [meth-]acrylamide derivative side chains must be included in the resulting biodegradable graft copolymers such that the bioactivity of the biological molecules of the backbone is not preserved and therefore the graft copolymers as described do not include polymer/protein bioconjugates. The Applicant has further amended claim 31 to specify that the biodegradable polymer is grafted with sufficient number of side chains selected from the group consisting of homo-oligomers of [meth-]acrylamide derivatives and co-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers such that said biodegradable thermally reversible graft copolymer forms a reversible gel. The Applicant has thus made plain in the specification, and in the claims, that the Applicant's biodegradable polymer does not include the non-gelling biologically active polymer/protein bioconjugates of Hoffman.

Closure

Applicant has made an earnest attempt to place the above-referenced

application in condition for allowance and action toward that end is respectfully requested. In the alternative, the Applicant respectfully requests that the Examiner enter the foregoing amendments to place the Application in better form for appeal. Should the Examiner have any further observations or comments, he is invited to contact the undersigned for resolution.

Respectfully submitted,



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Gutowska	Art Unit: 1711
Serial No: 09/209,541	Examiner: Jeffrey Mullis
Filed: 12/11/98	Paper No: 16
For: REVERSIBLE GELING CO-POLYMER AND METHOD OF MAKING	File No: E-1537-CIP
	Date: April 25, 2002

Box RCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Version of Amended Specification/Claims to Show Changes Made

The paragraph bridging pages 11 and 12, and beginning on page 11, line 26 and ending at the end of page 12 was replace with the following where underlined matter was inserted and [bracketed] matter deleted:

In addition to the nonresorbable reversible gel composed of a linear random copolymer of N-isopropyl [meth-]acrylamide and [meth-]acrylic acid described in this invention, a biodegradable (resorbable) copolymer exhibiting similar gelation properties is obtained by grafting of the oligo [meth-]acrylamide derivative side chains on a biodegradable polymer of, e.g., polyaminoacids, poly(phosphasenes), poly(caprolactone), polypeptides, polysaccharides and combinations thereof. As described above, in order to form a gel, a sufficient number of oligo [meth-]acrylamide derivative side chains must be included in the resulting biodegradable graft copolymers such that the bioactivity of the biological molecules of the backbone is not preserved and therefore the graft copolymers as described do not include polymer/protein bioconjugates. Preferred oligo [meth-] acrylamide derivative side chains include N-alkyl

substituted [meth-]acrylamide derivatives, linear random copolymer of [meth-]acrylamide derivative and hydrophylic comonomer, and combinations thereof. Techniques of grafting of oligo-N-isopropyl[meth]acrylamide side chains on a nonbiodegradable pH-sensitive homopolymer are described (Chen and Hoffman). The technique(s) of Chen and Hoffman were used herein to graft the oligo-N-isopropyl[meth]acrylamide side chains on an alternative biodegradable polymers such as polyaminoacids, poly(phosphasenes), poly(caprolactone), polypeptides, polysaccharides and combinations thereof. The first step of the synthesis is either the free radical homopolymerization or the random copolymerization of the oligo-N-isopropyl[meth-]acrylamide side chains by free radical polymerization using an aminoterminated chain transfer agent, for example 2-aminoethanethiol hydrochloride. The next step is the coupling of the amino-terminated macromer to the carboxyl moieties of the biodegradable polymer using the activation reagent, e.g., dicyclohexyl carbodiimide. Other biodegradable polymers such as poly(phosphazenes) poly(caprolactone), polypeptides, polysaccharides and combinations thereof may also be grafted with the oligo-N-isopropyl[meth-]acrylamide side chains using similar synthetic techniques. [The reaction solvent is non-aqueous, preferably a hydrocarbon, for example chloroform, dichloromethane, N,N-dimethylformamide or combinations thereof.]

Claim 31 was amended as follows where underlined matter was inserted and [bracketed] matter deleted:

31. (twice amended) A biodegradable thermally reversible graft copolymer, comprising:

a. a biodegradable polymer; grafted with
b. a sufficient number of side [chain] chains selected from the group consisting of homo-oligomers of [meth-]acrylamide derivatives and co-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers
c. such that said biodegradable thermally reversible graft copolymer [forming] forms a reversible gel.